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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,101	12/30/2005	Akira Kato	0425-1236PUS1	6760
2292 7590 02/05/2009 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747				
EXAMINER				
SOROUSH, ALI				
ART UNIT		PAPER NUMBER		
1616				
NOTIFICATION DATE		DELIVERY MODE		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary

Application No.

10/563,101

Applicant(s)

KATO ET AL.

Examiner

ALI SOROUSH

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-11,13-15,17-22 and 24 is/are pending in the application.
- 4a) Of the above claim(s) 18-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-11,13-15,17 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Acknowledgment of Receipt

Applicant's response filed on 10/28/2008 to the Office Action mailed on 07/28/2008 is acknowledged.

Status of the Claims

Claims 1, 5, 6, 10, 13-15, and 24 are currently amended, claims 2, 12, 16, 23, and 25 are cancelled, and claims 18-22 are withdrawn. Therefore, claims 1, 3-11, 13-15, 17, and 24 are currently pending examination for patentability.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1, 3-11, 13-15, 17, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-11, 13-15, 17, and 24 recite "good solvents" and "poor solvents", however it is not clear from the claims or the specification what would constitute a "good

solvent" and what would constitute a "poor solvent". Therefore, these terms are indefinite and fail to provide the metes and bounds of the aforementioned solvents.

Response to Applicant's Arguments

Applicant argues that the terms "good solvent" and "poor solvent" are art recognized terms commonly used by those skilled in the art. Applicant's arguments have been fully considered but found not to be persuasive. Applicant has listed US Patents 6531490, 6455238 and 6087471 as evidence that pervious patents have been issued using the same terms. It is the Examiners position that each patent application is examined on its own merits. Further Applicant argues that the specification makes the meaning of the terms clear. It is Examiners position that applicants specification makes unclear what constitutes a "good solvent" over what constitutes a "poor solvent". For example a water soluble drug would be highly soluble in water but not an organic solvent such as acetonitrile. However, a water insoluble drug is not soluble in water but is in an organic solvent. Applicant generally claims drug particles and therefore in each instance the definition of a "poor solvent" and "good solvent" changes relative to the properties of the drug. For the foregoing reasons the instant rejection of claims 1, 3-11, 13-15, 17, and 24 is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1, 3-11, 13-15, 17, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chaubal et al. (US Patent Application 2004/0245662, Published 12/09/2004, Filed 11/07/2003) in view of Feldmann (US Patent 2652234, Published 09/15/1953).

Applicant Claims

A method of producing ultrafine drug particles comprising the steps of: dissolving a drug in a good solvent, mixing the drug suspension in a poor solvent, and subjecting the mixture to high-pressure homogenization. Wherein the mixing occurs such that the poor solvent is circulated into the homogenizer and then the drug-containing solution is added to the circulating solution.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Chaubal et al. teach, a "[m]ethod for preparing submicron particles of antineoplastic agents." (See title). "The particles generally produced have an average particle size of less than about 1000 nm and are not rapidly soluble." (See abstract).

"Preferably the organic compound or the pharmaceutically active compound is poorly water-soluble. What is meant by 'poorly water soluble' is a solubility of the compound in water of less than about 10 mg/ml, and preferably less than 1 mg/ml." (See paragraph 0046). "The process for preparing the particles can be separated into four general categories. Each of the categories of processes share the steps of: (1) dissolving an organic compound in a water miscible first solvent to create a first solution, (2) mixing the first solution with a second solvent of water to precipitate the organic compound to create a pre-suspension, and (3) adding energy to the pre-suspension in the form of high-shear mixing or heat, or a combination of both, to provide a stable form of the organic compound having the desired size ranges defined above. The mixing steps and adding energy step can be carried out in consecutive steps or simultaneously." (See paragraph 0053). "The energy-addition step involves adding energy through sonication, homogenization, countercurrent flow homogenization, microfluidization, or other methods of providing impact, shear or cavitation forces ... In one preferred form of the invention, the energy addition step is effected by a piston gap homogenizer such as one sold by Avestin Inc. under the product designation EmulsiFlex-C160." (See paragraph 0077). In a preferred embodiment, "2.08 g of carbamazepine was dissolved into 10 mL of NMP [N-methyl-2-pyrrolidinone] . 1.0 mL of this concentrate was subsequently dripped at 0.1 ml/min into 20 ml of a stirred solution of 1.2% lecithin and 2.25% glycerin ... The predispersion was next homogenized cold ... for 35 minutes at 15,000 psi. The pressure was increased to 23,000 psi and homogenization was continued for another 20 minutes." (See paragraph 0142). "The method ... further compris[es] removing the

liquid phase of the suspension to form a dry powder of the particles." (See claim 27). "[W]herein the removing of the liquid phase is selected from the group consisting of: evaporation, rotary evaporation, lyophilization, freeze-drying, dia-filtration, centrifugation, force-field fractionation, high-pressure filtration, and reverse osmosis." (See claim 28). For the foregoing reasons the instant method is anticipated.

***Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)***

Chaubal et al. does not anticipate the mixing step such that the poor solvent is circulated into the homogenizer and then the drug-containing solution is added to the circulating solution. However, Chaubal et al. makes such a step obvious.

Chaubal et al. does not teach a homogenizer with an online injector. This deficiency is cured by the teachings of Feldmann.

Feldmann teaches, "the matter to be homogenized ... is forced by means of any suitable injector or pump ... into the feed channel and through the spiral ducts defined by the rib or ribs." (See column 2, Lines 49-54).

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art to perform the mixing of the two solutions such that the poor solvent is circulated into the homogenizer and then the drug-containing solution is added to the circulating solution. One would have been motivated to do so because Chaubal et al. teach that the mixing and energy addition can be done simultaneously. Therefore, if one wanted to perform the steps in

one more efficient way one would have been motivated to do mix and emulsify the solutions with in the homogenizer.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Sjostrom et al. with Feldmann. One would have been motivated to do so because Feldmann teaches that the injector is useful in feeding the solution to homogenized into the microfluidizer.

For the foregoing reasons the instant method would have been obvious to one of ordinary skill in the art at the time of the instant invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ali Soroush whose telephone number is (571) 272-9925. The examiner can normally be reached on Monday through Thursday 8:30am to 5:00pm E.S.T.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number For the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ali Soroush
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Art Unit: 1616

/Mina Haghighatian/
Primary Examiner, Art Unit 1616